IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Government of the United States,
As represented by the Secretary of the Army

Inventor(s) Kenneth Sherman, et al. Technology Center: 1600

Appln. No.: 09/544,108 Group Art Unit: 1648

Filed: April 6, 2000 Examiner: Boesen, A.

Title: COMPOSITION AND METHOD OF TREATING HEPATITIS C

APPEAL BRIEF

TABLE OF CONTENTS

Identification page	1
Table of Contents	2
Real Party In Interest	4
Related Appeals and Interferences	5
Status of Claims	6
Status of Amendments	7
Summary of Claimed subject matter	8
Grounds of Rejection to be reviewed on appeal	9
Arguments	10-13
Claims appendix	14
Evidence Appendix	15
Related Proceedings Appendix	16

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In re: PATENT APPLICATION of
Inventor(s) SHERMAN, et al.

Technology Center: 1600

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Examiner: Boesen, A.

Title: COMPOSITION AND METHOD OF TREATING HEPATITIS C

Hon. Commissioner of Patents
and Trademarks
PO Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL

Sir:

Responsive to the Final Office Action dated December 31, 2007 and Advisory Action dated April 15, 2008, please consider the following remarks:

(i) REAL PARTY IN INTEREST

The real party in interest is the United States Government as represented by the Secretary of the Army.

(ii) RELATED APPEALS AND INTERFERENCES

There are no related appeals and interferences.

(iii) STATUS OF CLAIMS

Claims 1, 3-6 and 25 are pending and finally rejected in the application.

Claims 2 and 7-24 have been cancelled.

(iv) STATUS OF AMENDMENTS

There are no amendments after final rejection.

All amendments to date have been entered.

(v) SUMMARY OF CLAIMED SUBJECT MATTER

The present invention is directed to a method of treating a mammal infected with Hepatitis C virus by administering an anti-hepatitis C viral effective amount of at least one α-interferon concurrently or sequentially with administering thymosin-α or a fragment of thymosin-α. (page 12, lines 1-4, page 13, lines 1-5, page 15, lines 15-25, page 16, lines 1-13,) The Appellant has found that improved results against Hepatitis C are achieved with a combination therapy over using either α-interferon alone or Thymosin alone.

The α-inerferon may be interferon α-2b (page 16, line 1-2).

The step of administering the α-interferon can be administering α-interferon produced by recombinant DNA technology (page 16, line 1-2).

The mammal may be a human (page 12, lines 23-26), and the amount of the α-interferon administered ranges between about one million and about three million units of the interferon per administration (page 16, lines 1-15, page 23, lines 1-5). The dose of thymosin α-1 can be about 1500 to about 1700μg of said thymosin α-1 (page 23, lines 6-8).

In the method of the invention, the fragment of thymosin-α is selected from the group consisting of C-terminal 4-28, C-terminal 15-28, N-terminal 1-8, N-terminal 1-14 and N-terminal 1-20. (page 13, first paragraph, lines1-5)

(vi) GROUNDS FOR REJECTION TO BE REVIEWED ON APPEAL

Whether claims 1, 3-6 and 25 are patentable over Huang (Virologica Sinica, 1990, vo. 5, p. 69-73) in view of Hoofnagle et al. and Moody et al. (U.S. Patent No. 5,273,963).

(vii) ARGUMENT

The present invention is directed to the treatment of Hepatitis C. Hepatitis C is caused by an RNA virus. For Hepatitis C, the injury is caused by the virus itself. The Applicant has found that improved results are achieved with a combination therapy over using either α-interferon alone or Thymosin α alone with this type of virus. None of the cited references, whether taken alone or together suggest the use of α-interferon together with Thymosin α as a suitable and effective means for treating Hepatitis C.

Discussion of the References:

Huang et al. is directed to a composition for treating Hepatitis B rather than Hepatitis C. Huang et al. combines α-interferon and thymosin to treat Hepatitis B. Huange et al. examines antigens and antibodies of HBV and HBcAg, DNAP, HBV-DNA. Huang, et al. is silent about Hepatitis C virus, antigens and antibodies. Huang, et al. is also careful not to speculate that its treatment for Hepatitis B would be useful for any other type of virus that attacks the liver or other disease forming viruses known to man.

In Hepatitis B, the injury is caused by the immunologic response to the virus. Hepatitis C virus does not hurt the liver by the immunologic response to the virus. In Hepatitis C, the virus itself attacks the liver. Given the different modes of operation of the two types of viruses, it cannot be stated based on Huang, et al. that a therapy for one virus would be effective against the other totally different type of virus.

The present method claims call for treating Hepatitis C by administering to a mammal an anti-Hepatitis C viral effective amount of at least one α-interferon, concurrently or sequentially with administering a thymosin α or fragment of thymosin α. Huang et al. does not indicate that thymosin is useful for treating Hepatitis C or the provide the preferred dose. Therefore, Huange et al. does not lead the artisan to the claims of the invention or treatment for any other RNA virus like Hepatitis C. Therefore, the composition of Huang, et al. does not render obvious the present claims, especially when there is no suggestion or assumption that could have been made to use the claimed ingredients together to treat Hepatitis C.

Hoofnagle, et al. does not make up for the deficiencies of Huang, et al. Hoofnagle et al. discloses a composition containing only α-interferon for treating

Hepatitis C. There is no mention of the use of thymosin for treating Hepatitis C or the combination of α-interferon with thymosin for treating Hepatitis C. There is no disclosure that a treatment for Hepatitis B would work for Hepatitis C or vise versa. There is no disclosure that Hepatitis C and Hepatitis B are similar viruses. There is also no suggestion of what the proper dosage unit of thymosin would be or what parameters would be useful to achieve the proper dosage unit of thymosin for the combination therapy of the claims for Hepatitis C. Although, Hoofnagle, et al. briefly discusses using *other antiviral agents or corticosteroids* in treating Hepatitis C in patients with suspected Hepatitis C who have not responded to alpha interferon, Hoofnagle, et al. does not suggest using immune system potentiating agents for treating Hepatitis C (page 261, col 2, last paragraph). Thymosin is not an antiviral agent or corticosteroid as these terms are used in the art. Without any motivation or assumption possible from Hoofnagle et al. to use an immune system potentiating agent such as thymosin to treat Hepatitis C, Hoofnagle, et al. would not have lead the skilled artisan to the present invention.

Moody is directed to compositions and methods for treating small cell and non-small cell lung cancers, not viruses, not Hepatitis C virus. Moody indicates that thymosin and interferon operates to treat the endogenous biochemical factors that regulate the growth of lung cancer cells. Moody has been cited to show that thymosin fragments have been identified to have "therapeutic significance." "Therapeutic significance" does not establish a prima fascia case of obviousness in the present application's claims.

Not only is there no combined therapy in Moody for treating Hepatitis C virus, there is no use of a combined therapy for the treatment of any other viral entity.

Therefore, Moody does not add to the disclosures of the above two references in such a way that would have motivated one of ordinary skill in the art to try thymosin with α-interferon to treat an RNA virus like Hepatitis C.

Applicant states that a doctor of ordinary skill in the art would not have automatically combined therapies of antiviral agents and immune potentiating agents for a particular disease without a great deal of experimentation because of the fear of side effects or the canceling of effectiveness or otherwise. It is respectfully submitted that the combination of Huang, et al., Hoofnagle, et al. and Moody would not have motivated one of ordinary skill in the art at the time of the invention to arrive at the present claims under

35 USC §103(a). Unexpected results have been shown by the Applicant and, therefore, this rejection should be withdrawn.

The Examiner has failed to show a reference that teaches thymosin-α to treat Hepatitis C. That is because no one before the filing of this application used thymosin-α to treat Hepatitis C. The Examiner has also failed to show a reference that suggests that the Hepatitis C virus would be affected by thymosin-α or that an immune system in a patient struggling with Hepatitis C infection could be improved by using thymosin-α. The Examiner has also failed to show that a combination therapy of α-interferon and thymosin-α would have the desired results in alleviating the Hepatitis C virus.

Rather, the Examiner has maintained that since α-interferon and thymosin-α have been used to treat cancer and Hepatitis B (a completely different type of virus that operates completely differently), it would have been obvious to use them together to treat Hepatitis C. The Examiner also maintains that the immunopotentiating effects of α-interferon in combination with thymosin α have been known to the artisan at the time of the invention.

Let's explore the Examiner's position carefully.

To make a prima facia case for combining references, the references should have some suggestion or teaching to make the combination. Here, none of the references make the suggestion for using the claimed ingredients to treat Hep. C or any other virus

If there is no suggestion, than the Examiner must establish that the combination is a predicable use of prior art elements according to their established function and it would have been predictable that the combined elements would have a therapeutic effect for Hepatitis C. The Examiner can not use mere hindsight.

It was not known at the time of the invention whether α-interferon in combination with thymosin α would have the same effectiveness in treating Hep C as they had in treating Hep B. It was **not predictable or obvious to try because of the fear of side effects and canceling of one drug by the other**. Extensive testing had to be performed to determine effectiveness. If the two ingredients were known at the time of the invention to have immunopotentiating effects for viruses other than Hepatitis B, than why did not every doctor and scientists in the world use the two ingredients together to treat cancer, every disease and every virus or at least every virus that attacked the liver? The

viruses that cause the mumps, measles, herpes and infectious mononucleosis also attach the liver and the combination therapy is not used and was not used for these viruses prior to the present invention.

It would have been simply too large of a leap in science to assume at the time of the invention, based on the cited references, that just because two ingredients work for one virus, they would have worked in the human body against every other virus in the same way.

As previously stated, a scientist experienced with Hepatitis B and Hepatitis C knows that Hepatitis C is caused by an RNA virus and Hepatitis B is caused by a DNA virus (emphasis added). These two types of viruses operate differently in a host. About 30% of persons with Hepatitis B show no symptoms. About 80% of persons with Hepatitis C show no symptoms. Hepatitis C is less likely than the other Hepatitis viruses to cause serious illness at first (only one-quarter of the people infected actually develop symptoms). There is a vaccine for preventing Hepatitis B that is available for all age groups that prevents Hepatitis B virus infection (available sine 1982). There is no vaccine for preventing Hepatitis C. No generalized assumption would have been made by one of ordinary skill in the art that a vaccine that works for one type of Hepatitis would work for the other type. Further, no generalized assumption could have been made at the time of the invention that a therapy that works for Hepatitis B would also work for Hepatitis C and that there would be no side effects that would prevent the combination in that particular illness.

Reconsideration and allowance of the claimed invention is respectfully requested.

Date: 6/27/08

Respectfully submitted,

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(viii.) CLAIMS APPENDIX

Claim 1. (previously presented) A method of treating a mammal infected with Hepatitis C virus, comprising administering to said mammal an anti-Hepatitis C viral effective amount of at least one α-interferon, concurrently or sequentially with administering a thymosin-α or fragment of thymosin-α.

Claim 2. (Canceled)

Claim 3. (Previously presented) The method of claim 1, wherein said α- interferon is interferon α-2b.

Claim 4. (Previously presented) The method of Claim 1, wherein the step of administering said interferon comprises administering interferon produced by recombinant DNA technology.

Claim 5. (Previously presented) The method of Claim 1, wherein said mammal is a human, said interferon is an α-interferon, and the amount of said interferon administered ranges between about one million and about three million units of said interferon per administration.

Claim 6. (Previously presented) The method of Claim 1, wherein said mammal is human, said thymosin is thymosin α-1, and said dose is about 1500 to about 1700 μg of said thymosin α-1.

Claims 7-24 (cancelled)

Claim 25. (previously presented) The method of claim 1, wherein said fragment of thymosin-α is selected from the group consisting of C-terminal 4-28, C-terminal 15-28, N-terminal 1-8, N-terminal 1-14 and N-terminal 1-20.

Claim 26. (cancelled)

(ix.)EVIDENCE APPENDIX

I. The Declaration signed December 19, 2005 by Dr. Kenneth Sherman and filed with the Patent Office on January 2, 2006 established efficacy of the claimed method and pharmaceutical composition. The Applicants showed to the PTO that improved results were achieved with a combination therapy over using either α-interferon alone or thymosin-α alone. These results were unexpected by the Applicant because no one prior to this invention had even suggested using thymosin-α for the treatment of Hepatitis C let alone a combination therapy. Hence, the first part of the Examiner's final rejection that no improved results have been demonstrated is not true.

(x) RELATED PROCEEDINGS APPENDIX

None